BioNanoScience (2018) 8:963–970
https://doi.org/10.1007/s12668-018-0562-z

Spatial Structure and Conformational Mobility of Seven-Membered Cyclic Acetals and Ketals Containing Pyridoxine Moiety in Solution by NMR Methods

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Published online: 19 September 2018

Abstract
In the last decade, pyridoxine derivatives were widely used for the synthesis of molecules with important biological and physical properties. However, rational synthesis of the compounds with desirable biochemical or physical properties often requires information about their spatial structure and conformational mobility. NMR spectroscopy is a powerful tool for conformational analysis of biologically important samples, such as pyridoxine derivatives, in solution. This paper is devoted to a review of the results obtained by our group over the last 5 years on the NMR study of nine newly synthesized pyridoxine derivatives in acetone solution. It was shown that studied compounds are involved into several conformational exchange processes. The activation energies of all observed conformational exchange processes were calculated.

Keywords Pyridoxine · Dynamic NMR · Conformational exchange · Structure · Stereochemistry

1 Introduction

In the last decade, acetal and ketal derivatives of pyridoxine were widely used for the synthesis of the molecules with important biological and physical properties [1–5]. Furthermore, these compounds had been also reported as novel organic nonlinear optical materials [6, 7]. These materials exhibit physicochemical properties suitable for second harmonic generation. The possibility of creating efficient lasers based on the synthesized compounds directly depends on their physical and chemical properties, which are closely related to the three-dimensional structure of the molecules. Therefore, study of spatial structure and molecular dynamics of these compounds in solution is a problem of current interest. These compounds contain various substituents at the ortho position of the seven-membered cycle (Fig. 1). Both of them—the substituent and the cycle—participate in fast relative to the NMR time-scale conformational exchange processes creating a complicated stereochemical picture. It is well known that seven-membered cyclic acetals and ketals with planar fragments exist in solution in dynamic equilibrium of two conformations: the chair and the twist [8–11]. Previous studies revealed some correlations between steric structure and reactivity of these compounds [12–14]. Information about molecular dynamics of these compounds will help to understand mechanisms of their action and provide the ways to design the structures with improved activity.

Compounds **I**–**IV** contain seven-membered acetal ring with 2,4-dinitrophenyloxy ortho-substituent (Fig. 1). This molecular configuration provides a good opportunity to study the influence of the dinitrophenyl fragment's rotation around the pyridine-oxygen bond on the conformation of the acetal ring, which is involved in the fast relative to the NMR time-scale conformational exchange process at room temperature. Compounds **V** and **VI** contain the same 2,4-dinitrophenyloxy ortho-substituent, but the substituents at the ketal carbon atom are different. This distinction leads to significant differences in conformational transformations of seven-membered ring. The influence of the dinitrophenyl fragment's rotation around the C12-O bond on the conformation of the ketal ring was also studied. The compounds **VII**–**IX** contain a seven-membered ring with a 2-nitrophenyl ortho-substituent attached to pyridine fragment. In these cases, the rotating group connected to the pyridine ring by single C9–C15 bond which makes it less flexible. Consequently,

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s12668-018-0562-z) contains supplementary material, which is available to authorized users.

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